EVALUATION OF PERSISTENT PNEUMONIA AND PERCUTANEOUS NEEDLE ASPIRATION OF LUNG AS A TOOL IN THE ETIOLOGICAL EVALUATION OF CHILDREN WITH PERSISTENT PNEUMONIA

Dissertation Submitted for

MD DEGREE EXAMINATION

BRANCH VII - PEDIATRIC MEDICINE

INSTITUTE OF CHILD HEALTH
AND
HOSPITAL FOR CHILDREN
MADRAS MEDICAL COLLEGE
THE TAMILNADU Dr.M.G.R. MEDICAL UNIVERSITY
CHENNAI.

SEPTEMBER 2006

CERTIFICATE

Certified that this dissertation entitled **"EVALUATION OF PERSISTENT PNEUMONIA AND PERCUTANEOUS NEEDLE ASPIRATION OF LUNG AS A TOOL IN THE ETIOLOGICAL EVALUATION OF CHILDREN WITH PERSISTENT PNEUMONIA"** is a bonafide work done by **Dr.G. SRINIVASAN, M.D.,** Post Graduate Student of Pediatric Medicine, Institute of Child Health and Hospital for Children, Egmore, Chennai - 600 008, during the academic year 2003 - 2006.

Prof.Dr.R.Duraisami, M.D. D.C.H.,

Prof. of Pediatrics
Institute of Child Health and
Hospital for Children,
Madras Medical College,
Chennai.

Prof.Dr.S.Sethuraman,M.D., D.C.H., D.M.I.T.,

Prof. of Pulmonology
Institute of Child Health and
Hospital for Children,
Madras Medical College,
Chennai.

Prof. Dr. Mangayarkarasi Senguttuvan M.D.,DCH.,

Director and Superintendent,
Institute of Child Health and
Hospital for Children
Madras Medical College, Chennai.

Prof. Dr. Kalavathi Ponniraivan B.Sc., M.D.,

The Dean,
Madras Medical College,
Chennai.

DECLARATION

I declare that this dissertation entitled **"EVALUATION OF PERSISTENT PNEUMONIA AND PERCUTANEOUS NEEDLE ASPIRATION OF LUNG AS A TOOL IN THE ETIOLOGICAL EVALUATION OF CHILDREN WITH PERSISTENT PNEUMONIA"** has been conducted by me at the Institute of child health and Hospital for Children, under the guidance and supervision of my unit chief **Prof.Dr.R.Duraisami, MD., DCH.**, and the head of department of Pulmonology, **Prof.Dr.S.Sethuraman, M.D.,DCH.,D.M.I.T.** It is submitted in part of fulfillment of the award of the degree of M.D (Pediatrics) for the September 2006 examination to be held under the Tamil Nadu Dr.M.G.R Medical University, Chennai. This has not been submitted previously by me for the award of any degree or diploma from any other university.

(Dr. G. Srinivasan)

SPECIAL ACKNOWLEDGEMENT

My sincere thanks to **Prof. Dr. Kalavathi Ponniraivan, B.Sc., M.D.,** the Dean, Madras Medical College for allowing me to do this dissertation and utilize the institutional facilities.

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to **Prof.Dr.Mangayarkarasi Senguttuvan M.D., D.C.H.,** Professor of Pediatrics, Director and Superintendent of Institute of Child Health and Hospital for Children for permitting me to undertake this study.

I am extremely thankful to **Prof.Dr.R.Duraisami, M.D., D.C.H.,** Professor of Pediatrics and our unit chief for his guidance, invaluable help, encouragement and support throughout the study.

I am extremely thankful to **Prof.Dr.S.Sethuraman, M.D., D.C.H., D.M.I.T.,** Head of the Department of Pediatric Pulmonology for his guidance, invaluable help, encouragement and support throughout the study.

I would like to thank our unit Assistant Professors, **Dr.M.Raghunathan M.D., D.C.H., Dr.M.Rathnasamy, M.D., D.C.H., Dr.V.E.Vivekanadan, M.D., D.C.H., and Dr.Mekalai Suresh Kumar, M.D., D.C.H.,** for their valuable guidance and support in doing this study.

I am greatly indebted to **Dr.D.Vijayasekaran, M.D., D.C.H., Ph.D., and Dr.N.C.Gowrishankar, M.D., D.C.H.,** Asst. Professors of Pulmonology Department for their invaluable support and guidance without which this study could not have been possible.

I would like to thank **Dr.M.Mohammed Meeran, M.D., (Micro) M.D.,D.V.,** Professor of Microbiology for his help in executing this study.

I extend my sincere thanks to **Dr. Uma Devi, M.D., (Microbiology)** for her valuable help and guidance in doing this work.

I extend my sincere thanks to **Dr. Senthamarai, M.D.,** Retired Professor of Pathology for her valuable help and guidance in doing this work.

I extend my sincere thanks to **Dr. Kothainayagai, M.D., D.C.H., and Dr.P.Ramachandran, M.D., D.C.H.,** Registrars for their valuable suggestion and guidance in doing this work.

I sincerely thank all the children and their parents who have submitted themselves for this study without whom this study would not have been possible.

CONTENTS

INTRODUCTION

Parenchymal lung diseases are a significant cause of morbidity and mortality, both in the devoloping as well as the devoloped world,especially in children.World wide pneumonia is estimated to cause the death of four million children under five years of age annually[1].While acute lower respiratory tract infections remain the most important cause of morbidity and mortality in the under fives in the devoloping countries, persistent and recurrent pneumonias are not uncommon.

The incidence of all respiratory tract infections in devoloping countries varies from 4.2-8.7 per child per year[2,3]. However the incidence rates of pneumonia are much lower about 10 per 1000 children per year[2,3].Though only a small fraction of these turn out to be persistent pneumonia,still they contribute to a significant proportion of morbidity and mortality. No community studies have reported the incidence of persistent or recurrent pneumonia[4].

Persistent pneumonia implies a chronic non resolving pneumonia.They often manifest as acute lower respiratory tract infections and continue to persist for a varying period of time, irrespective of the treatment.Sporadic reports reveal various aspects of this important disease which often baffles the peadiatricians,patients and parents.

Many different entities are known to either influence or to cause pneumonia that is persistent. Commonly encountered conditions like asthma,tuberculosis and foreign bodies can give rise to persistent lung infiltrates[5].Swallowing abnormalities and gastroesophageal reflux can give rise to recurrent aspiration,

leading on to persistent pneumonia.Some children experience persistent pneumonia as a result of deficiencies in the local pulmonary or systemic host defences or from underlying lung disorders that modify the lung defences[5].Congenital malformations of the airways may predispose the child to recurrent aspirations leading on to pneumonia. Congenital anomalies of the lung like sequestration,hypoplasia and cystadenomatoid malformations may also act as the underlying cause of persistent lung infiltrates[5.]Anomalies of the cardiovascular system, especially left to right shunts increase the risk of recurrent and persistent pneumonia[5].Non infectious disorders like hypersensitivity pneumonitis, pulmonary haemosiderosis and sickle cell disease may be responsible for persistent lung infiltrates in a small fraction of cases[5].Persistent lung infiltrates pose a significant challenge to the paediatricians.Persistent pneumonia is a diagnostic challenge rather than a therapeutic dilemma.

In view of the changing pattern of the etiological agents responsible for pneumonia in childhood, it is essential to identify the etiological agent.The etiological diagnosis is essential in a overwhelming majority of clinical conditions that require specific therapy.

Various techniques have been used to study these infections but none seems to be ideal.Moreover paediatricians are limited in their ability to make a specific etiologic diagnosis because sputum is not usually available,results of throat cultures may be unrevealing and results of nasopharngeal cultures are frequently misleading because of high carrier rates of respiratory pathogen in this age group[6].Though lung aspiration is a simple and the most direct way to

obtain a specimen from lung parenchyma without risk of any contamination to identify the etiologic agent, it is hardly practiced.

Compared to other invasive procedures like transbronchial lung biopsy, thoracoscopic lung biopsy and open lung biopsy, percutaneous needle aspiration is a minimally invasive procedure with good safety records that can provide adequate tissue sample for microbiological and cytological studies[7].Percutaneous needle aspiration is a useful tool in the identification of the etiological agent in persistent pneumonia [7].

Frequent occurrence of persistent pneumonia in children required further studies to enlighten the various aspects of this disease that remain a diagnostic challenge to the paediatricians throughout the world.

REVIEW OF LITERATURE

Definition

Pneumonia is defined as the inflammation of lung parenchyma, the portion distal to the terminal bronchiole comprising the respiratory bronchiole, alveolar ducts, sacs and alveoli. Although the inflammation may have many different causes and varying duration, the term pneumonia most commonly refers to acute inflammation.

John Crofton [8]says the term pneumonia indicates an inflammation, in general, acute of the substance of the lung.The normally sterile lung may be invaded by bacteria, viruses, mycoplasma,fungi,protozoa and virtually every other known forms of microbiologic organisms.All of these induce inflammation of the lung, known as pneumonia.

The anatomic pattern of the inflammatory reaction depends, as would be expected, on both the host and the invader.Thus bacterial pneumoniae tend to induce intraalveolar exudation resulting in consolidation of the lung parenchyma.If the consolidation is patchy, it is referred to as broncho pneumonia.Some organisms may induce confluent and massive, sometimes total, lobar consolidation of the lungs, producing what is called lobar pneumonia.However certain bacteria cause not only consolidation but also simultaneous focal necrosis of the lung architecture (lung abcess).In contrast to the bacterial infections,viruses or mycoplasma evoke usually interstitial inflammation.

Eggleston et al[9] .discussed pneumonia as a non specific term and argued that it is difficult to make the distinction among subsegmental atelectasis, pneumonitis and non specific bronchovascular associated densities. Thus the diagnosis of pneumonia is apt to be made when a radiodensity is present but the exact nature of the lesion is not known.

Crompton et al[10]. classified pneumonia etiologically into the primary pneumonia in which the disease is caused by a specific pathogenic organism and the secondary pneumonia in which some abnormality of the respiratory system predisposes to the invasion of the lung by the organisms of low virulence and secondary infection generally reaches the alveoli by aspiration from other parts of respiratory tract.

The diagnosis of persistent pneumonia implies that the pneumonic infiltrate seen on chest x-ray have not resolved in the expected course of time. Similarly the diagnosis of recurrent pneumonia can be made only if a normal chest skiagram is obtained between the episodes of illness. It is difficult to determine whether the pneumonia is truly persistent or recurrent .In normal host the speed of the radiographic resolution depends on the etiologic agent and may vary from two weeks with respiratory syncytial virus or parainfluenza virus to as long as 12 months with adenovirus infection. Pneumoccal pneumonia normally clears in 6-8 weeks[11,12,13].Densities that clears in hours or in one to two days are likely to be subsegmental ateclectasis and not infectious pneumonia.

Somu et al.[14] defines **persistent pneumonia** as persistence of pneumonic infiltration in the chest skiagram for more than four weeks even after effective antibiotic therapy. **Recurrent pneumonia** is defined as the presence of

radiologic pneumonic infiltrates in the same child at varying intervals with clearance of radiological lesion in between the episodes.

Wald et al.[15]defines **persistent pneumonia or non-resolving pneumonia** as persistence of symptoms and radiographic abnormalities for more than one month.

There is no consensus on the definition of persistent pneumonia[5]. **Persistent pneumonia** implies a chronic, non-resolving pneumonia. It is defined as persistence of symptoms and radiographic abnormalities for more than one month[15].However, some authors prefer to use the cut off of three months[5].The speed of radiographic resolution depends on the etiologic agent. Therefore, it is difficult to arrive at one particular cut-off for defining persistent pneumonia[5].

One has to mention about the term slowly resolving pneumonia and non resolving pneumonia when dealing with persistent pneumonia. Rome et al [16] conducted a study on **non resolving pneumonia** where they state that any patient with pneumonia whose radiograph has failed to resolve by 50% in two weeks or completely in four weeks should be considered to be non resolving or slowly resolving. Oren Lasker[17] defines **slowly resolving pneumonia** as persistence of symptoms and radiographic abnormalities beyond the expected time course.

Lung defence mechanisms

The lungs are protected by an elegant defence system aimed at preventing potential pathogens from reaching this site and at containing and eliminating the organism that do gain entry.

Anatomical features of the upper airway contribute to the first line of defence[18].It starts with the upper airway, the nasal turbinates and the sharp angular turn from the naso and oropharnyx into the posterior pharnyx acts as a baffles where inhaled particles can impact. The ciliated cells move a mucus layer which floats on a solute layer to the back of the throat and is swallowed. Mucus contains complex glycoproteins called mucins that trap microorganisms. Binding of the pathogen to the respiratory tract epithelium is prevented by decreased mucosal pH, secretory IgA and the constant desquamation of epithelial cells[18].In addition the nasopharynx is colonised with non pathogenic bacteria that can interfere with the attachment of the pathogen to the host cells.

Entry to the lower respiratory tract is protected by glottis. If secretion do enter the lower respiratory tract they can be cleared by coughing. In the lower respiratory tract non specific defences include macrophages, fibronectin, lysozymes, lactoferrin, IgG, defensins, collectins and complement[18]. Alveolar macrophages play a role in both innate and acquired immunity. The immunoglobulins contribute to humoral defence mechanisms. IgA present in high concentration in the upper respiratory tract protects against viral infections. It is less abundant in the lower respiratory secretions, where it may help agglutinate bacteria, neutralise the bacterial toxins and reduce bacterial

attachment to mucosal surfaces. IgG in the serum agglutinates and opsonises bacteria, activates complements, promotes chemotaxis of granulocytes and macrophages,neutralises bacterial toxins and viruses and lyses Gram negative bacteria. Also present on the alveolar surface are alveolar macrophages which ingest and kill organisms. Lymphocytes producing humoral and cell mediated immunity, migrate from blood stream to parenchyma to help combat infection.

The various factors involved in the lung defence mechanism are given in the table[19].

Physical and physiological defences	**Secretory defences**
Airway filtration of particles	Immunoglobulins G,A,M and E
Cough	Collectins
Sneezing	α-1antitrypsin,
Bronchoconstriction	β-2 macroglobulin
Mucociliary clearance	Lysozyme
Airway mucus	Lactoferrin
Respiratory cilia	Complement
Alveolar fluid movement	α and β Defensins
Cellular defences	Interferons
Lymphocytes(T and B cells)	
Pulmonary macrophages	
Neutrophils	

Etiology

Persistent pneumonia usually result from deficiencies in the local pulmonary or systemic host defenses or from underlying disorders that modify the lung defences. Drug resistant infections are on the rise, especially in a nosocomial infection. Wrong choice of antibiotics or inadequate duration of therapy may be the sole cause of persistent pneumonia. The underlying disorders associated with these infections can be broadly classified into the following categories[5.]

Congenital malformations of the upper or the lower respiratory tract, and congenital heart diseases especially left to right shunts.

Conditions predisposing to recurrent aspiration.

Defects in the clearance of airway secretions, especially cystic fibrosis and ciliary abnormalities.

Disorders of systemic/local immunity.

Table I shows the probable causes of recurrent or persistent pneumonia. Congenital malformations of the airway may predispose the child to repeated aspirations, leading on to pneumonia. Congenital anomalies of the lung such as sequestration, hypoplasia and cystadenomatoid malformation of the lung may also act as the underlying cause of recurrent or persistent pneumonia. Anomalies of the cardiovascular system especially left to right shunts increase the risk of persistent and recurrent pneumonia.

Table I - Etiologic Factors for Recurrent or Persistent Pneumonia[5]

A.Congenital Malformations

1. Airways

   Cleft palate

   Pierre Robin syndrome

   Tracheoesophageal fistula

   Tracheomalacia.

2. Lungs

   Pulmonary hypoplasia

   Pulmonary sequestration

   Congenital cystadenomatoid malformation

   Bronchogenic cyst.

3. Cardiovascular

   Congenital heart diseases, especially left to right shunts

   Vascular rings.

B.Aspirations

   Gastro-esophageal reflux

   Swallowing abnormalities

   Foreign body

   Anomalies of the upper airways.

C. Defects in the clearance of airway secretions

Cystic fibrosis

Abnormalities of the ciliary structure and function

Abnormal clearance secondary to infections, repair of congenital defects.

Airway compression both intrinsic & extrinsic e.g., mediastinal tubercular lymphadenopathy.

D. Disorders of local/systemic immunity

Primary immunodeficiencies

Acquired immunodeficiencies

HIV Infection

Immunosuppressive therapy

Malnutrition.

E.Allergic disorders like bronchial asthma, eosinophilic pneumonitis

F.Infection with resistant organism like tuberculosis ,fungus.

G.Improper and inadequate treatment of infections and resistant infections.

Recurrent or chronic aspirations may be associated with anomalies of the upper airway, abnormal swallowing mechanisms, gastro-esophageal reflux (GER) or neuromuscular disorders[20]. Aspirations alter the pulmonary host defenses[21]. Defects in clearance of airway secretions may be because of

abnormalities of respiratory mucus as in cystic fibrosis or defects in mucociliary function - which may be due to structural defects of cilia or secondary to various infections[22].Compression of the airway both intrinsic and extrinsic interferes with the clearance of airway secretions[23].

Various inherited and acquired disorders of immunity predispose the child to respiratory infections, in addition to infection at other sites. Occasionally, disorders of immune system may be localized just to the lungs. Severe malnutrition and deficiency of trace elements such as zinc may predispose a child to various infections. However, the exact role of these in recurrent and persistent lower respiratory tract infections is not well studied[24].

Non-infectious disorders such as asthma, hypersensitivity pneumonias, pulmonary hemosiderosis, and sickle cell disease may be responsible for recurrent or migrating lung infiltrates. Persistent lung infiltrates may also be caused by congenital anomalies such as lung cysts, cystadenomatoid malformations and sequestration, even in the absence of infection. Pulmonary hemosiderosis, hypersensitivity pneumonitis, sarcoidosis, interstitial pneumonitis, alveolar proteinosis, collagen vascular diseases and eosinophilic pneumonias are also associated with persistent lung infiltrates. These conditions should be considered in a child with recurrent or persistent lung infiltrates, if infection seems unlikely[5]. History and clinical examination may offer clues for these conditions.

There is scant data available on the causes of recurrent or persistent pneumonia in children. Most of the available literature is from the west, with hardly any information from the developing countries.

Eigen et al.[25] could identify a definite etiology in only 20 of 81 children referred for recurrent or persistent pneumonia. 8 of these 20 had significant neuromuscular dysfunction or mental retardation or both. In 61 children without any apparent cause, 18% had wheezing during initial visit, 31% had a history of wheezing and 49% had a history of allergy or family history of asthma. This study suggested that asthma is a common cause of persistent or recurrent pneumonia in children and that this may occur as the initial symptom even in the absence of wheezing.

Eighteen Saudi children were evaluated for etiology of persistent or recurrent pneumonia[26]. Immune and inherited metabolic disorders were found in 44.4% and anatomic abnormalities in four (22.2%). None of the children had tuberculosis, pertussis or cystic fibrosis.

There are very few published data on etiology of persistent or recurrent pneumonia in children in India[5].One hundred and fifty seven children were evaluated for recurrent or persistent pneumonia (excluding left to right shunts and tuberculosis) during 1996-98 in the Pediatric Chest Clinic at All India Institute of Medical Sciences, New Delhi[5]. Structural abnormalities of upper and lower respiratory tracts were observed in 40 children(25.47%). 41 children(26.11%) were diagnosed to have cystic fibrosis, while 21(13.37%) had recurrent aspirations due to various causes. 21 children(13.37%) were immunodeficient, of whom 17(10.82%) had HIV infection. Asthma was diagnosed in 8 children(5.09%). No etiology could be determined in 19 children(12.10%). This pattern may not be representative as this is based on a biased sample of referred patients. Cystic fibrosis may have been over-

represented because of the availability of diagnostic facilities for the same at the institute. The studies from the west have not listed cystic fibrosis as a cause possibly because it is diagnosed more readily and early, and are treated separately.

Again there are few systematic data available on the etiologic organism responsible for persistent pneumonia in Indian scenario. A study by Kumar et al[27] in 30 episodes of pneumonia in 27 children with malignancy on chemotherapy to assess etiology, done using percutaneous needle aspiration of lung, showed an underlying cause in 53.3% of the episodes. Organisms isolated included Pseudomonas, Klebsiella, E.coli, Streptococcus faecalis and Diphtheroids.

Tuberculosis is likely to be an important cause of persistent pneumonia especially in countries like India[28].The common organisms responsible for acute lower respiratory tract infections may also be the responsible agents for recurrent infections in a child who is immunocompetent. Infections with Cytomegalovirus and Chlamydia may also lead to persistent infiltrates. However, immunocompromised children are more likely to be infected with atypical organisms such as Pneumocystis carinii, fungi, Legionella, etc[24].

The paucity of clinical datas in India emphazises the need for further studies in this area. While tuberculosis is probably the most important cause of persistent pneumonia in devoloping countries, it is usually diagnosed early and easily, given the high index of suspicion. Whether the causes of persistent pneumonia in our country are similar to those seen in the devoloped countries or not remains an unanswered question.

Pathogenesis

Organisms reach the lung to cause pneumonia by one of the following four routes.

a. Inhalation of microbes present in the air.

b. Aspiration of organism from the naso or oropharynx.

c. Hematogenous spread from a distant focus of infection

d. Direct spread from a contiguous site of infection or penetrating injury.

Anaerobes generally are of low virulence to humans. Multiplication and invasion are favoured by any process which creates a more favourable environment by removing oxygen or by adding reducing substances which lower the oxidation reduction potential. In some cases removal of aerobes facilitates anaerobic invasion.

Fungal infections are becoming common and some of them are serious and fatal. With the control of most bacterial infection in the devoloping countries, fungal infections have assumed greater importance. Human fungal infections are mainly oppurtunistic. Modern advances in treatment such as antibiotics, steroids and immunosupressive agents have also led to an increase in oppurtunistic fungal infections[29].

The most common event disturbing the defence mechanism of lung is a viral infection that alters the properties of normal secretions, inhibits phagocytosis,

modifies the bacterial flora and may temporarily disrupt the normal respiratory epithelial layer.

Children with defects in the defence mechanisms or in the chain of event involved in the recovery of infections experience recurrent pneumonia or fail to resolve the disease completely. The defects in the immune system which could lead to persistence of pneumonia has already been mentioned.

Clinical approach

Since respiratory tract infections (mostly upper tract) are common in early childhood, it is important to be sure about the site of infection before a child is subjected to the detailed work up for persistent pneumonia. It is important to differentiate persistent from recurrent pneumonias. This problem may be sorted out by a careful assessment of the history and physical examination. There is also a need to separate out the cases of just chronic cough, without any features suggestive of infection of the lower respiratory tract.

Often differentiation between recurrent and persistent infections may be difficult. The issue may be sorted out if sequential radiographs of the chest are available. It is also important to recognize that persistent radiographic abnormalities may be present because of atelectasis and non-infectious disorders like asthma, hypersensitivity pneumonitis, pulmonary hemosiderosis and interstitial lung disease. Before proceeding to the investigations, a good history and physical examination are mandatory. There are several features that may help in reaching a diagnosis.

1. **Age of onset**

Onset of symptoms soon after birth increase the possibility of the presence of hereditary/congenital disorder. Congenital malformations such as tracheoesophageal fistula, cystic adenomatoid malformation and congenital lobar emphysema present early in life. Disorders of humoral immunity usually present in later infancy.

2. Details of the episodes

A detailed account of the episode of pneumonia should be obtained. Onset, nature and duration of cough, occurrence of fever, documentation of signs of lower respiratory tract infection by a physician, radiographic evaluation, type and duration of antimicrobial therapy (adequate/appropriate), response to therapy and the need for hospitalization should be recorded in detail.

The parents should be asked about the timing of the symptoms in relation to feedings and the change in position, vomiting, irritability, and nocturnal symptoms of coughing and wheezing. In a child with depressed cough reflex, coughing or gagging may be minimal or absent. Sleep disturbances may be seen in gastro-esophageal reflux and obstructive lesions, especially of upper respiratory tract[20].

3. Past history/Associated complaints

Occurrence of repeated infections at other sites should be asked for. A positive history may suggest systemic immunodeficiency. The type of infections may give a clue to the type of immunodeficiency[24],for e.g., recurrent respiratory or

gastrointestinal infections may indicate an underlying IgA deficiency. History of foreign body inhalation should be elicited. Diagnosis of tuberculosis in the past should not be ignored. History suggestive of malabsorption may be present in cystic fibrosis. History suggestive of bad child rearing practice like exposure to irritant fumes, oil bath, nose blowing etc. should be specifically asked for, especially in younger children and infants.

4. Perinatal history

Prematurity, a diagnosis of bronchopulmonary dysplasia in the neonatal period or prolonged exposure to oxygen and its attendant complications, maternal infections, and blood transfusions should be asked for. Occurrence of meconium ileus or delayed passage of meconium should arouse suspicion of cystic fibrosis. History of excessive secretions/drooling might alert one towards esophageal atresia with tracheo-esophageal fistula. History suggestive of cyanosis, feeding difficulties,suck-rest-suck cycle and respiratory distress should all be enquired to rule out congenital heart diseases.

5. Family history

It is important to enquire about any family history of allergic disorders, asthma, cystic fibrosis, and congenital anomalies. Occurrence of recurrent infections in other family members may suggest immunologic disorder. An inquiry about the high risk behavior or history of blood transfusion in parents is essential, to rule out exposure to maternal HIV infection, in a child where immunodeficiency is suspected.

6. Environmental history

Risk factors for sources of exposure to respiratory infection should be evaluated. Exposure to inhaled pollutants, irritants and passive tobacco smoking should be carefully assessed[30].A mention about the condition of the house where they live in and whether adequately ventilated or not, should be made.

Physical examination

The aim of the physical examination is to document presence of respiratory disease, localize the site of infection, and to detect any underlying etiologic factor.

General physical examination should include evaluation of growth and development, and inspection for clubbing of the fingers or toes. Clubbing may be present in chronic suppurative lung diseases like lung abscess, bronchiectasis and conditions like cystic fibrosis and bronchiolitis obliterans[31]. The patient should be assessed for lymphadenopathy, presence/ absence of tonsillar/adenoidal tissue. Tonsils may be absent in hypo/agammaglobulinemia. Generalized lymphadenopathy may be present in tuberculosis, HIV infection, and histiocytosis[5].

Respiratory system examination includes assessment of respiratory rate, evidence of distress, thoracic deformities, wheezing, stridor, the dimensions of the chest and careful auscultation of the chest to localize the infection. Evaluation of nose, paranasal sinuses and ears is mandatory. Nasal polyposis

may be an important clue to cystic fibrosis. Recurrent middle ear infection may occur in immuno-deficiency syndromes and ciliary dyskinesia syndromes[5].

As left to right shunts (anomalies of cardiovascular system) predispose to recurrent lower respiratory infections, these should always be looked for. Dextrocardia may offer a clue to immotile cilia syndrome. Chronic hypoxemia due to chronic pulmonary disorder may lead to cor pulmonale[32].

The palate, tongue, and oropharynx should be inspected for any anomalies. Whenever the diagnosis of aspiration is considered, observation of the child during feeding is essential. Nasopharyngeal regurgitation, difficulty in sucking/swallowing and associated coughing/choking should be looked for[33]. Central nervous system should be examined to look for conditions like cerebral palsy, mental retardation and infantile hypotonic states which are associated with neuromuscular incordination leading on to difficulties in swallowing and recurrent aspiration.

Based on history and physical examination, the severity of the disorder can be assessed. The following features suggest a severe disorder[5]: (i) Failure to thrive; (ii) Limitation of activity; (iii) Persistent fever; (iv) Persistent tachypnea and respiratory distress; (v) Persistent hyper-inflation; (vi) Significant/sustained hypoxemia; and (vii) Persistent radiographic abnormalities. Presence of clubbing, growth retardation, increased A-P diameter of the chest indicate chronicity of the disease/infection.

It is difficult to construct an algorithm for assessment of a child with persistent pneumonias because of the wide range of causes. It is important to consider each case individually to decide the plan of investigations accordingly[28].

Investigations

Investigations should be planned after careful evaluation of the history and examination findings. As the causes of persistent pneumonia are so many,the child should be investigated judiciously. It is absolutely necessary to rule out tuberculosis ,gastroesophageal reflux and underlying cardiovascular diseases before proceeding to further investigations[28].The diagnosis of TB may be suggested by a positive contact history, a positive tuberculin test and chest radiography. The diagnosis is confirmed by Zeihl-Nielson staining, culture for acid fast bacillus and other investigations available. A fine needle aspiration of the lymph node is done if an associated tuberculous enlargement of the lymph node is suspected.

WBC counts may not be helpful as lymphocytosis may be a feature of any chronic or partially treated infections. Esonophilia may suggest an allergic disorder. High erythrocyte sedimentation rate may be a feature of tuberculosis, malignancy or collagen vascular diseases.

Radiographic evaluation of the of the chest is essential for the localisation of the infiltrates, their extent and resolution over time in any child having persistent pneumonia[11].Large pulmonary densities with an airbronchogram suggests consolidation, while those without airbrochogram, but with mediastinal shift may be due to mass lesion. Specific areas of pulmonary

infiltrates should be identified in all chest x-rays. Right upper lobe involvement suggests chronic aspiration in younger children and right lower lobe is involved more often in aspiration in older age group. Right middle lobe often results from extrabronchial compression and lower lobe infiltrates may be due to an underlying bronchiectasis. Presence of infiltrates in the same localized area is by obstruction by a foreign body or congenital anomaly while infiltrates due to chronic infection have an irregular shaggy borders[5].Infiltrates that are more likely to occur in different lobes or segments are more likely to be seen in generalised disorders such as immunodeficiency states. Chronic or linear infiltrates are seen with infection such as cytomegalovirus, pnemocystis cariini,HIV or non infectious conditions like sarcoidosis, histiocytosis or granulomatosis[34]. Parenchymal shadows are differentiated from pleural or mediastinal shadows on the basis of distribution of the lesion. Parenchymal shadows are usually restricted to a lobe or segment while extrapulmonary shadows are not restricted by any such boundary. Cardiac silhoutte might suggest a primary cardiac defect.

A barium swallow is done in all children to rule out gastroesophageal reflux(GER) or other conditions associated with abnormalities in swallowing.If needed they are confirmed by upper gastrointestinal endoscopy. While demonstration of GER is easy, documentaton of GER as a cause for recurrent or persistent pneumonia is difficult.

Computed tomography of the chest is particularly useful in diagnosing structural anomalies such as cysts, sequestration lung, congenital lobar

emphysema, tumors and presence of enlarged lymph nodes[5].It also helps in defining the extent of involvement of the lung.

Bronchoscopy in indicated if abnormality of bronchial anatomy or foreign body aspiration is suspected[5].In addition bronchoalveolar lavage can be performed in an attempt to identify the etiologic agent. Presence of lipid laden macrophages in bronchial washings has been found to be of value in confirming recurrent or chronic aspiration. Quantification of lipid laden macrophages in bronchial washing is a better marker of aspiration[33] . Radionucleotide salivagram can identify chronic salivary aspiration."Milk technetium scan" may demonstrate aspiration[5].

Sweat chloride estimation should be performed if feasible in all children with recurrent or persistent pneumonia[5]. While, earlier, cystic fibrosis was thought to be extremely rare in India, its presence is being increasingly recognized. Cystic fibrosis is an important cause of recurrent or persistent pneumonia and is probably underdiagnosed[5].

Most children referred because of recurrent pneumonias do not have specific immunologic defect. Various minor defect have been identified in these children . In the present scenario, when the prevalence of HIV infection is rapidly increasing in our country, effort should be made to look for risk factors for HIV infection[5].

A systemic immunodeficiency is suspected if in addition to recurrent pneumonia, there is evidence of infection at other sites e.g., skin, gut, etc. The presence of other features of the recognized specific immunodeficiency

syndrome provides supportive evidence for disorders of systemic immunity. The initial investigations includes complete and differential blood counts, quantitative serum immunoglobulins and skin tests of delayed hypersensitivity. Further investigations may include T and B cell subset quantification. If phagocytic defects are suspected, screening tests include neutrophil count and nitroblue tetrazolium test[5].

Percutaneous lung aspiration

In 1883, Leydon and Gunthu[35] described the first recoveries of Diplococci, identified by staining from the lung of living patients suffering from pneumonia. However by 1905, exploratory thoracic puncture had become so enthusiastically employed that a British authority felt compelled to editorialise most strongly against the indiscriminate use of the procedure citing 11 deaths,7 of them in children. However the technique employed was not fully described .Chronic respiratory infections comprised the bulk of the clinical material and sudden cardio-respiratory inhibition with or without attendant haemorrage was the typical complication observed.

Horden[36] in 1909, presented a bacteriological study of 14 patients stating clearly the indications for the procedure and fully described the technique. He observed that the procedure will frequently reveal the existence of a mixed infection when this is not suspected. No complications were observed.

The first large series of pneumonia in infants and children studied by lung puncture was that of Lyon in Boston in 1922[37].20 lobar and 18

bronchopneumonia patients were tapped yielding 55% rate of bacteriological diagnosis. Only two of the tapped children were under 3 years of age.

The risks of lung puncture in pneumonia were brought into proper perspective in 1936 by Sappington et al[38]. who could find only one instance of sudden death in reviewing 2000 lung taps .In their own series ,54 out of 68 taps in 60 instances of lobar pneumonia were bacteriologically positive.3 experienced hemoptysis (trivial in two) and one pneumothorax was observed. The operative techniques employed were well described but the bacteriological methods were not very clear.

In 1971 Mimica et al [39]reported a study of 543 lung taps in children with pneumonia.187 taps were positive.144 for Staphyloccus aureus,3 for S.epidermidis,5 for Pseudomonas,9 for E.coli,5 for Diplococcus pneumonia,12 for H.influenza and 9 for Klebsiella. Complications reported in 13 cases included 9 instances of pneumothorax and 4 haemoptysis.

In India in 1971,Shakuntala et al [40]published a series of 50 cases of lung puncture aspiration in acute pneumonia of newborn.31 cases had a positive yield,14 for Staphylococcus,2 for Streptococci,1 for Pseudomonas and 14 for Pneumococcus. Complications were reported in 3 cases.

Some of the recent studies in the subject includes the study of Elina et al.[41], from the hospital for children and adolescents, Helsinki university, Finland, who performed lung puncture in 34 children. Aspiration disclosed the etiology in 20(59%) cases and in 18(69%) of 26 patients, from whom a representative specimen was obtained. They concluded that lung aspiration has a high

microbiologic yield with a low risk of clinically significant adverse event and added that it should be used if the identification of the causative agent outweighs the modest risk associated with the procedure.

The study by Berger et al[42]. reported the value and safety of percutaneous lung aspiration in children with serious pulmonary infections who were either seriously ill or failed to respond to appropriate and adequate antimicrobial therapy.98 children were studied. Etiology was established in 60(61%) patients. In 18 cases the original therapeutic regimen had to be changed.11 complications encountered in 10 children included 9 instances of pneumothorax and 2 mild self limiting hemoptysis. There were no deaths. They concluded that it is a potentially useful and reasonably safe technique for the diagnosis of pulmonary infections in carefully selected cases when an exact etiologic diagnosis in needed.

The latest study on lung puncture in children from India was by Kumar and Bakshi[27] in 2004 from the paediatric department, AIIMS. Lung aspiration was performed to find out the etiology of pneumonia in 27 children with malignancy who were on chemotherapy. The yield was 53.3 %.One minor pneumothorax that resolved spontaneously was encountered. They concluded that it is a safe and useful procedure in immunocompromised persons with pneumonia who do not respond to the initial broad spectrum antibiotics.

Various authors have used different techniques for performing the lung puncture. Kumar et al.[27] used a 10 ml disposable plastic syringe and a 21 guage needle. In localised infiltration or consolidation the sites were selected

according to radiological assessment. In bilateral diffuse involvement the right 3rd or 4th intercostal space was used for lung aspiration[27].

As far as the complications are concerned, incidence of pnemothorax varying between nil and 10% are reported in various studies[42]. Pneumothorax which are severe enough to need chest tube drainage is reported in less than 3% of cases in most studies. Most pneumothoraces occur during or within the first hour after the procedure. Factors associated with an increased risk includes emphysematous changes within the lung, coughing, increased lesion depth, multiple pleural punctures, large bore needle and positive pressure ventilation[43].The majority of pneumothoraces which needs chest drainage are identified immediately following the procedure.

The incidence of hemorrage, another expected complication following the procedure, ranges between nil to 5 % in most studies[42].It is almost always self limiting. It usually manifests as hemoptysis. Patients with hemorrage should be placed puncture site down to decrease the risk of blood being carried to the opposite lung[42]. Other remote complications rarely encountered includes systemic air embolisation and secondary infection.

Table showing the **complications of lung aspiration** in various studies

Author	Total no. of cases	Nil complications		Pneumo - thorax		Hemoptysis	
		No.	%	No.	%	No.	%
Dinesh et al[45].	25	23	92	2	8	-	-
Mimica et al[38].	543	530	97.6	9	1.7	4	0.7
Diana et al[39].	31	27	87.1	3	9.7	1	3.2
Sakunthala et al[39.]	50	47	94	2	4.0	1	3.1
Elina et al[40].	34	34	100	-	-	-	-
Kumar et al[26].	27	26	96.29	1	3.71	-	-
Berger et al[41].	98	87	88.77	9	9.18	2	2.04

STUDY JUSTIFICATION

Persistent pneumonia contributes to a significant proportion of morbidity and mortality due to lower respiratory tract infections. Very few studies have been done in this field worldwide and most are from western countries. Being a tertiary referral center, a sizeable number of undiagnosed persistent lung infiltrates are reported to the Institute of Child Health, Chennai. Most children with undiagnosed lung disease would have been seen by a multitude of paediatric specialists and would have undergone a battery of baseline and hi-tech investigations prior to reporting to this hospital. The diagnosis still remains elusive inspite of extensive clinical work up, baseline & radiological investigations. Compared to the more invasive procedures like open lung biopsy, videoassisted thoracoscopic biopsy and transbronchial lung biopsies in children, percutaneous needle biopsy is a minimally invasive procedure that can provide adequate tissue sample for histopathological and microbiological examination, thus aiding immensely in the diagnostic work up of the children with persistent parenchymal lung disease. A number of studies[41]have proved that percutaneous needle aspiration is simple, reliable, economic and a minimally invasive procedure with very good safety records in trained hands.

The outcome of this study is expected to throw an additional light in the etiological evaluation of the perplexing problem of persistent lung infiltrates.

AIM OF THE STUDY

1. Diagnostic work up of children with persistent pneumonia

2. Percutaneous transthoracic needle aspiration of the lung as a tool in the etiological evaluation of children with persistent pneumonia where no underlying causes or contributory factors are found by other investigations.

MATERIALS AND METHODS

STUDY DESIGN: Descriptive study.

STUDY PLACE : Department of pulmonology,ICH & HC*, Egmore.

STUDY POPULATION:

Children between one month and twelve years of age with persistent pneumonia admitted in various units of ICH & HC*. The study sample was also obtained from other pediatric teaching hospitals in the city by informing them in advance regarding the nature and aim of study.

Inclusion criteria

1. Children between one month and twelve years of age with persistent pneumonia i.e.,persistence of signs & symptoms pertaining to respiratory tract along with radiographic abnormalities for more than four weeks.

2. Percutaneous transthoracic needle aspiration of the lung in children with persistent pneumonia where no underlying causes or contributory factors are found.

*Institute of child health and hospital for children

Exclusion criteria

Children under one month and more than twelve years of age were excluded from the study. The exclusion criteria for performing percutaneuous lung aspiration in a child with persistent pneumonia were[44]

Children with bleeding disorders.

Children with severe pulmonary hypertension, contralateral pneumonectomy.

Children with severe respiratory distress and poor general condition who cannot tolerate the procedure.

Children with suspected echinococcal cyst, possible arterio-venous malformations & emphysematous bullae in the anticipated path of the procedure.

Children with retrocardiac pneumonitis.

These children were excluded from study to avoid the remote risk of complications associated with this procedure.

Children with both Mantoux and contact positivity were not subjected to lung aspiration as they are emperically started on antituberculous drugs based on IAP* consensus guidelines.

* Indian Academy of Paediatrics

Manouevre

An informed consent was obtained from the parents or caretakers. Coagulation profile was done to rule out bleeding disorders as a part of preliminary work up. Anticoagulants and antiplatelet medications discontinued ideally for 7 days if the patient was already on them. An intravenous line, blood pressure monitor, ECG leads and an oxygen saturation monitor were placed. The procedure room was kept equipped with oxygen, suction, oral and nasal airways and an AMBU bag[44].Care was taken to ensure that all emergency drugs were readily available. Strict sterile precautions were taken before proceeding with the lung aspiration.

The lung aspiration consisted of making a percutaneous puncture into the portion of the lung shown by clinical and radiological examinations, the maximum pathological involvement. In case of bronchopneumonia, the right third or fourth intercostal space on the midclavicular line was used as the site of aspiration[27].An ordinary 10 ml plastic disposable syringe with a tightly fitting 22 / 24 guage needle, of length 1-1.5 inches, was used. The skin over the area was cleaned thoroughly with cetrimide and povidone iodine.One ml of sterile saline was taken in the syringe and the bevelled portion of the needle was then inserted underneath the skin at the upper border of the lower rib to avoid the neurovascular bundle. The needle was quickly inserted as far as required to hit the desired focus. Care taken to avoid striking the great vessels, heart and other viscera by tapping those areas which were anatomically determined to be safe. After reaching the desired focus, saline was injected and suction applied in an attempt to lavage the area. The needle was then withdrawn immediately

maintaining the negative suction pressure. Following the withdrawal of the needle, firm pressure was applied over the puncture site for around five minutes followed by a tincture benzoin seal, so as to provide an effective seal, thereby reducing the complication of pneumothorax.

The material thus aspirated was sent immediately for microbiological and cytological studies. The specimen sent for bacteriological diagnosis was immediately inoculated into the following media[45] (1) Sheep blood agar. (2) Chocalate agar (3) MacConkey's agar. (4) Potato dextrose agar with antibiotics and (5) Thioglycolate broth. The aspirate was also inoculated in Lowenstein Jenson medium and Seboraud's dextrose agar for isolation of mycobacterium and fungal species respectively. The aspirate was smeared and stained with Gram and Ziehl-Nielson stains and smears were also sent for cytological studies.

After the procedure the patient was placed puncture site down where possible to reduce the incidence of pnuemothorax. The vitals were assessed regularly for the next four hours and if stable, the child was transferred to the ward. A check x-ray was taken immediately after the procedure and was repeated whenever necessary to exclude the possibility of any clinically undetected complication.

OBSERVATIONS

Sixty nine children with persistent parenchymal lung infiltrates admitted in various wards of the hospital were analysed systematically with clinical features ,basic investigations and radiological evidences.

Age and sex distribution

Male children outnumbered female children with a ratio of 1.3:1. 39(56.5%) of the total number were male and 30(43.5%) were female children. Male children again outnumbered female children in the one month - one year age group. This disparity was less prominent among other age groups.

As far as the age incidence is concerned, a majority of them belonged to the under fives especially the under one age group.34 children(49.7%) fell under the age group one month to one year. The minimum age in the studied children was 3 months and the maximum was eleven and half years.

Table showing **age & sex distribution**

Age group	**Total cases (69)**		**Male children (39)**		**Female children (30)**	
	n	**%**	**n**	**%**	**n**	**%**
1 month- I year	34	49.27	20	51.28	14	46.66
1-2 years	9	13.04	4	10.25	5	16.66
2-5 years	14	20.28	8	20.51	6	20.0
5-12	12	17.39	7	17.94	5	16.66

Common symptoms

The majority of children had fever, cough, cold and breathlessness as the predominant presenting complaint. Irritability, poor feeding and failure to gain weight were the other common symptoms observed. History suggestive of recurrent aspiration or foreign body ingestion was not present in any child. Family history of asthma was not present in any child.

Table showing the **presenting symptoms**

Symptoms	**Total no. of cases**		**Average duration**
	n	**%**	
Cough	56	81.15	34 days
Breathlessness	59	85.50	32 "
Irritability	54	78.26	22 "
Fever	52	76.00	26 "
Poor feeding	23	33.33	38 "
Bad CRP	16	23.18	4 months
Failure to thrive	16	23.18	3.5 months

Bad CRP

At least one bad child rearing practice was present in 17 children who presented in infancy. Some of them had a combination of more then one bad child rearing practice. Male children were found to be at higher risk of bad

child rearing practice when compared to female children. Most children with H/O bad CRP* had an exposure to irritant fumes. H/O of nose blowing and oil instillation into nose were also present. Bad child rearing practice assumes importance because of the possibility of oil instillation/ nose blowing etc. leading on to lipoid pneumonia ,presenting as persistent lung infiltrates.

Children with bad CRP∗

Bad CRP*	**Total cases**		**Male children**	**Female children**
	n	%		
Nose blowing	3	18.75	2	1
Oil instillation	4	25.0	3	1
Irritant fumes	7	43.75	3	4
Native medication	5	31.25	2	3

∗child rearing practice

H/o - History of

Treatment details

All the children studied had received at least one antibiotic prior to recruitment.39(56.52%) had been exposed to two or more antibiotics and 19(27.52%) had been treated with 3 or more antibiotics .The mean duration of the antibiotic prior to recruitment was 24 days. Four children were emperically started on antituberculous drugs before reporting to the hospital.

Nutritional status

Malnutrition was found to be a common accompaniment with persistent pneumonia.42 children(60.86%) fell under the malnourished category according to Indian Academy of Paediatrics classification. A majority of them fell under the grade 1&2 categories. Five (7.28%) children belonged to the grade 4 category. The predominant age group which was found to be malnourished, was the under fives.

Classification based on IAP* grading

Grades	1mon-1 year		1-5 years		5-12 years	
	n	%	n	%	n	%
Normal	12	5.29	7	30.43	8	66.66
1	6	7.64	6	26.08	2	16.66
2	9	6.47	6	26.08	1	8.33
3	3	8.82	3	13.04	1	8.33
4	4	1.76	1	2.94	--	--

* Indian academy of paediatrics

Clinical features

The common clinical findings were dyspnea and tachpnea which were present in around 85-90% of the children. Fever was present in 47 (69.11%),crackles in 56(81.15%) and wheeze in 31(44.92%) children. Clubbing was present in 4

children(5.79%).3 children(4.34%) showed cyanosis. Cardiac murmurs were suspected in five children. 3 cases (4.34%) showed clinical features suggestive of septicaemia

Table showing **the clinical features**

Clinical features.	**No.of cases**	**%**
Tachypnea	62	89.85
Dyspnea	59	85.50
Crackles	56	81.15
Fever	47	68.11
Wheeze	31	44.92
Cardiac murmurs	5	7.24
Clubbing	4	5.79
Cyanosis	3	4.24
Septicemia	3	4.24
Hepatosplenomegaly	2	2.89

Tuberculosis screening

All 69 children were subjected for tuberculosis screening.7 children (10.14%) tested positive for Mantoux. A definite history of contact with an open case of tuberculosis within the past two years was present in 4 cases(5.79%).These children also showed Mantoux positivity .BCG* scar was present in all except 3

cases. Parental screening was negative in all screened cases. Resting gastric juice for acid fast bacillus was positive in 4 children(5.79%).In these cases Mantoux test and contact history were negative.

Tuberculosis screening

Screening	Positive		Negative	
	n	%	n	%
Mantoux.	7	10.14	62	89.85
Contact screening	4	5.79	65	94.20
Both Mantoux and contact positivity	4	5.79	65	94.20
RGJ* for AFB♦	4	5.79	65	94.20
BAL♣ for AFB	1	1.76	55	98.21
BCG # scar	66 (present)		3 (absent)	

*Resting gastric juice. ♦Acid fast bacillus.

♣Bronchoalveolar lavage # Bacillus Calmette Guerin.

Barium swallow and echocardiogram

Barium swallow revealed the presence of radiologically demonstrable gastroesophageal reflux in 3 cases(4.24%).One child showed features of achalasia cardia. They were later confirmed by upper gastrointestinal endoscopy. Echocardiogram was done in all the children to rule out congenital heart diseases .Ventricular septal defect was detected in 2,patent foramen ovale

in one and partial anomalous pulmonary venous connection in one. They were presumed to be the possible contributing factor for persistent pneumonia though they could not be directly implicated.

Radiological features

Radiological features were analysed in all the cases.23 showed features of consolidation, 39 of bronchopneumonia and 7 showed pneumonitis in the retrocardiac region. These 7 children were not taken up for lung aspiration in view of the retrocardiac location of the lesion.

Table showing the **chest skiagram pattern**

Findings	**No. of cases**	**%**
Consolidation	23	33.33
Bronchopneumonia.	39	56.52
Retrocardiac pneumonitis.	7	10.14

Eleven children underwent CT thorax. CT picked up one case of sequestration lung masquerading as persistent pneumonia.

Other investigations

Immunoglobulin profile was done in 11 children in whom an underlying immunodeficiency was suspected. The profile was normal in all of them. Sweat chloride test for cystic fibrosis was done in four patients and it was within normal limits. All 69 children were screened for HIV status. Two children

(2.89%)tested positive. Their parents were also found to be positive in HIV screening.

Bronchoscopy

Bronchoscopy was performed in 56 children excluding those children who showed both contact and Mantoux positivity and in whom resting gastric juice was positive for acid fast bacillus. Bronchoscopy showed evidence of pale mucosa and chronic inflammatory changes in 28 children. Purulent secretions were found in 23 cases. There were features suggestive of endobronchial tuberculosis like widening of the carina due to lymph node enlargement and presence of grayish white granulation tissues in the in the bronchial tree in 4 cases. These 4 children were negative for tuberculosis in all the earlier screening methods. Bronchoalveolar lavage showed the presence of acid fast bacillus in one child.

Airway anomalies like tracheomalacia and bronchomalacia were present in 2 cases. Vegetable foreign body was identified in 2 cases. One interesting case of Asperigillosis demonstrated by the presence of whitish fleeting masses was encountered in one child which was later confirmed by biopsy.

Table showing findings in **bronchoscopy**

Bronchoscopy findings	**n**	**%**
Normal study	19	33.92
Pale mucosa / chronic inflammatory changes	28	50.00
Purulent secretions	23	41.07
Features suggestive of endobronchial TB	4	7.14
Tracheomalacia & Bronchomalacia	2	3.57
Foreign body	2	3.57
Aspergillosis	1	1.78

Lung aspiration

Lung aspiration was done "in 34 cases where no possible etiology or contributory factors were found" in earlier mentioned investigatory modalities.7 children who showed pneumonia in the retrocardiac region were excluded based on exclusion criteria. In one child the procedure was not done because of severe respiratory distress and poor general condition.

Gram staining showed the presence of pus cells in 4 cases. Gram positive cocci was found in one and Gram negative bacilli in two cases. Yeast cells were identified in one case. The Zeihl-Neilson staining for acid fast bacillus was positive in one child. This child also showed growth of Mycobacterium Tuberculosis in culture. Cytological studies revealed the presence of lipid laden

macrophages in 5 cases(14.70%).These children also had a definite history of bad child rearing practice thus suggesting the possibility of lipoid pneumonia.

Lung aspiration results

Smear study

Findings	No.of cases
Presence of pus cells	4
Gram positive coccus	1
Gram negative bacilli	2
Yeast cells.	1
Presence of AFB	1

Culture studies

Bacterial culture of the aspirate showed the presence of klebsiella in four(33.33%), H.influenza in three(25%),Staphylococcus aureus in two(16.66%) and E.coli & Pseudomonas in one each(8.33%).There was no growth in 22 cases(64.70%).Fungal culture turned out to be negative in all the cultured specimens.

Organism isolated	Total no. of cases
H.influenza	3
Klebsiella	4
Staphylococcus aureus	2
Pseudomonas	1
E.coli	1
Mycobacterium tuberculosis	1
No growth	22
Fungal culture	--

Antibiotic sensitivity

The antibiotics were changed in five patients based on the sensitivity reports and in the rest of the cases, no changes were made as they were already started on the antibiotics sensitive to that particular strain. Change in the antibiotic resulted in the improvement of all the five children both clincally and radiologically. In general, the gram negative organisms were more sensitive to cephalosporins and aminoglycosides and gram positive S.aureus was more sensitive to ciprofloxacin and amikacin.

Antibiotic sensitivity pattern of culture positive cases

Name of the patient	Organism grown	Sensitivity pattern									
		Ampicillin	Gentamycin	Cefataxime	Ceftrioxone	Amikacin	Ciprofloxacin	Norfloxacin	Cotrimoxazole	Erythromycin	Ceftazidime
Rajeswari	Klebsiella	ns	ms	ms	ms	hs	hs	ns	ns	ns	ms
Sanjay	H.influenza	ns	ms	ms	ms	ms	ms	ns	ns	ns	ms
Somiya	Pseudomon	ns	ms	ns	ns	ms	ms	ns	ns	ns	hs
Rohit	H.influeza	ms	ms	ms	ms	ms	ms	ns	ms	ns	hs
Arun	Klebsiella	ns	ns	hs	ms	ns	ns	ns	ns	ms	ns
Surya	S.aureus	ns	ns	ns	ns	ms	ms	ns	ns	ms	ns
Gopikrisna	S.aureus	ns	ms	ns	ns	hs	hs	ms	ns	ns	ns
Manikanda	Klebsiella	ns	ns	ns	ns	hs	ms	ns	ns	ns	ns
Saran	H.influenza	ms	ms	ns	ns	ms	ns	ms	ms	ns	hs
Satish	H.influenza	ns	ns	ms	ms	ns	ms	ms	ms	ns	ms
Babu	E.coli	ms	ms	ms	ms	ms	ns	ms	ns	ns	ms

hs-highly sensitive, ms-moderatively sensitive, ns-not sensitive

The antibiotics were changed in five patients based on the sensitivity reports and in the rest of the cases, no changes were made as they were already started on the antibiotics sensitive to that particular strain. Change in the antibiotic resulted in the improvement of all the five children both clinically and radiologically. In general, the Gram negative organisms were more sensitive to

cephalosporins and aminoglycosides and Gram positive S.aureus was more sensitive to ciprofloxacin and amikacin.

Complications

Among 34 cases who underwent percutaneous lung aspiration, only one case of self limiting hemoptysis was encountered. Air leak complications were not seen in any case. There were no deaths associated with the procedure.

Follow up

During follow up, around 50% of the cases showed symptomatic improvement. Another 23% showed both symptomatic and radiological improvement. There was no improvement in 6 children and 5 out of these had lipoid pneumonia. 11 children were lost during follow up and 2 children died due to sepsis out of which one had a coexisting HIV infection.

Follow up results

Result	Total no. of cases	1 mo-one year	1-5 years	5-12 years
Symptomatic improvement	34	18	9	7
Symptomatic plus radiological improvement	16	4	10	2
Improvement after antibiotic change	5	3	2	--
Lost during follow up	11	6	3	2
No improvement	6	4	1	1
Died	2	2	--	--

DISCUSSION

Persistent pneumonia implies a chronic non resolving pneumonia. Though there is no universal consensus on when to label pneumonia as persistent, the presence of symptoms and radiographic abnormalities beyond a period of one month, should raise the possibility of an abnormal predisposing condition. The correct identification of the predisposing cause and its appropriate treatment is the cornerstone in the management of these children. The underlying disorder associated with these infections can be due to congenital malformations of the upper or lower respiratory tract, cardiovascular system, recurrent aspirations, defects in the clearance of the airway secretions, ciliary abnormalities and disorders of systemic or local immunity which may be congenital or acquired.

There are few reports on the underlying causes of persistent pneumonia in children. Most of the reports are on recurrent pneumonia. Some authors have discussed about recurrent and persistent pneumonia together. There are no recent reports regarding lung aspiration in children with persistent pneumonia. The study done by Kumar et al[27] in AIIMS was on children with malignancy on chemotherapy with persistent lung infiltrates.

In this study, children presenting within the first year of life accounted for around 50% of the patients while another 33% presented between 1-5 years age group. Only 17% of the children were above 5 years of age. In the study conducted by Lodha et al[28] in children with persistent pneumonia, the reported age distribution was similar. Male children contributed to 56.5% of the cases in our study. Lodha et al reported an even greater disproportion in sex distribution, male children comprising nearly 80%.

In this study the etiological work up revealed that tuberculosis still comprises a majority of cases of persistent pneumonia. It accounted for around 20% of the total cases. Recurrent aspiration due to various causes like gastroesophageal reflux and achalasia cardia accounted for 5.8 % of the total cases. HIV infection, leading on to systemic immunodeficiency was probably the cause for persistent pneumonia in around 3% of the cases. Aspergillosis, foreign body aspiration, congenital airway anomalies and sequestration lung accounted for another 6% of the cases studied. Congenital heart diseases with left to right shunts could be a possible contributory factor in around 6% of the cases as they could not be directly implicated as a cause for persistent pneumonia. Lipoid pneumonia as evidenced by the presence of lipid laden macrophages in the lung aspirate and bronchial washings accounted for another 7% of the cases. No specific contributory factors were found in 40 cases(58%).

Lung aspirate was carried out on children, where no possible underlying causes or contributory factors were found. The technique used in this study was similar to the one adopted by kumar et al[27].Lung aspirate revealed the bacterial cause for pneumonia in around 32% of the cases. The common isolates were klebsiella (32.33%), H.influenza(25%) and Staphylococcus aureus (16.66%).Fungal culture was negative in all the cases. The smear study showed the presence of Gram positive organism in one and Gram negative species in two cases. The discrepency between the culture result and the gram staining result might be due to observer variation. The lung aspirate culture results correlated with the blood culture result in 3 cases and with the bronchoalveolar culture in 2 cases, reinforcing the fact that the same organism may not always be responsible in both infections.

Tuberculous etiology was identified in one case as the cause of persistent pneumonia(2.94%).It was interesting to note that this child was negative for tuberculosis in all the other preliminary tuberculosis related investigations carried out.

No organisms were isolated in 64.70% of the cases after lung aspiration. This may be due to the non infectious causes of pulmonary infiltrates, viral causes or other fastidious organisms which requires special media. It has to be remembered that even after a procedure as invasive as open lung biopsy the diagnosis may not be possible in upto 20% of the cases[27].

The lung aspiration conducted by Kumar et al [27]in children with malignancy on chemotherapy showed a bacterial cause in around 53% of the cases and the organisms commonly encountered in their study were Pseudomonas, E.coli and Klebsiella. The yield was higher because of the more sophisticated microbiological methods used by them. The Gram staining and AFB staining were not contributory in their study.

The lung aspiration results modified the treatment pattern in five children which resulted in their improvement both clinically and radiologically. Antituberculous drugs were started in one child following isolation of acid fast bacillus in the lung aspirate.

As far as complications are concerned, pneumothorax which is reported in various studies, was not encountered in our study probably because we used a finer guage needle when compared to other studies and probably because of the firm pressure and effective seal applied at the puncture site. Hemoptysis was

observed in only one child which was managed conservatively. There were two death which were unrelated to the procedure. The absence of significant complications indicate the safety of the procedure.

CONCLUSION

Persistent pneumonia occurs predominantly in the under-five age group and more so in infancy. Male children were affected slightly more frequently than their female counterparts. The male female ratio was 1.3:1.

The common complaints in the children were cough, fever, breathlessness, irritability, poor feeding and failure to thrive. The common clinical features were fever, tachpnea, dyspnea and the presence of crackes on auscultation. Malnutrition was found to be a common accompaniment.

Bad child rearing practice was a possible contributory factor, especially in children below one year, leading on to lipoid pneumonia which presented as persistent lung infiltrates.

Foreign body, congenital airway anomalies and anatomical lung abnormalities commonly presented as consolidation on x-ray chest whereas immunodeficiencies and lipoid pneumonia presented as diffuse infiltrates.

As tuberculosis still accounted for around 20% of the total cases presenting as persistent lung infiltrates, we may be justified in starting emperical anti tuberculous drugs when the etiology remains clueless.

Foreign body aspiration, congenital heart diseases, gastroesophageal reflux, swallowing abnormalities, anatomical lung abnormalities etc. should all be kept in mind while evaluating a case of persistent lung infiltrates. HIV screening should be done in all cases.

Lung aspiration revealed a specific bacterial etiology in 32% of the cases. There was a predominance of gram negative organisms in the culture. The lung aspiration also identified one case of tuberculosis which was not detected in other earlier investigations.

The diagnostic yield could have been higher if modern microbiological methods for isolation of viruses, anaerobic organisms, and culture for organisms like Chlamydia, Mycoplasma and Legionella were used.

As far as the safety of lung aspiration is concerned, this study has reinforced the fact that it is a relatively safe procedure when done with finer guage needles in trained hands and is fraught with complications only in rare instances.

The results of the lung aspiration modified the treatment in five cases resulting in the betterment of the patient. Antituberculous drugs were instituted in one child leading to the resolution of pneumonia. Thus this procedure might be helpful in a small minority of children were etiology remains clueless.

The study has also shown that this procedure is a simple and the most direct way of obtaining a specimen from lung parenchyma without the risk of contamination from other floras.

Finally to conclude, the lung aspiration should be done if the advantages of a specific etiologic diagnosis outweighs the small risk associated with the procedure .It should be attempted in the small group of children with persistent pneumonia when trained hands and a good back up is available.

PROFORMA
ANNEXURE

1. Name 2. Age/Sex 3. Sr no.

4. Father's name 5. I.P No.

6. Address

7. Clinical features at initial presentation

8. Treatment given with duration

9. Cheif complaints at present with duration

10. Symptoms in the intervening period

11. Past history

12. H/o bad CRP

13. Perinatal history

14. Family history

15. Contact history with TB

16. Nutritional history

17. Environmental history

18. Immunization history

19. Physical examination
    General examination Anthropometry
    Vital signs
    RS
    CVS
    ABD
    CNS
20. Radiological findings

21. Barium swallow findings

22. CBC

23. ESR

24. Mantoux test

25. Family screening for TB

26. RGJ for AFB

27. HIV status

28. Echocardiogram

29. Bronchoscopy

30. BAL

31. UGI scopy*

32. CT chest*

33. Sweat chloride estimation*
34. Immunoglobulin assay*

35. Lung aspiration study

    Gram staining and smear study
    Bacterial c/s
    AFB culture
    Fungal culture

36. Final diagnosis

37. Follow up

* In Selected Cases

BIBLIOGRAPHY

1. WHO-The world health report,1995. Bridging the gaps.Geneva:WHO;1995.

2. Selwyn BJ on behalf of the coordinated group of the Bostid researchers. The epidemiology of the acute respiratory tract infections in young children; comparison of findings from several devoloping countries. Rev. infec. dis. 1990:12(suppl.8)S 870-S 888.

3. Pio, Leowshi J, Tendim Her.,The magnitude of the problem of acute respiratory infections. In ARI in childhood. eds. Douglas M, Kerby Eaton E.Proceedings of an international workshop. Sydney, Australia: Aug. 1984 : Univ of Adelaide.1984:3-17.

4. Owayed AF, Campbell DM, Weng E.Underlying causes of recurrent pneumonia in children:Arch.paediatric adolesc. med.2000.154:190-4.

5. Lodha SK, Kabra, Dept. of paediatrics,AIIMS.Recurrent and persistent pneumonia.Indian peadiatrics 2000:37:1085-1092.

6. Barlett JG, Breimann RF, Mandella et al.,Community acq pneumonia in children and adolescents. Clin. infc. dis.26:811:1998.

7. The value and complications of percutaneous transthoracic lung aspiration for the etiologic diagnosis of community acquired pneumonia,Scott&Hall-116(6)1716-chest.

8. Crofton & Douglas Respiratory diseases.ed.Seaton,Blackwell publishers; vol.2:p.823-878.

9. Eggleston PA, Wald BH, Pierson WE et.al.,Radiographic abnormalities in acute asthma in children.Paediatrics:54:442:1974.

10. Crompton GK, Grant WB, Mackardy, In Davidson's principles and practice of medicine. ed. John Macleod. 14th ed.p.22.

11. Osborne D.The radiological appearance of viral disease of the lower respiratory tract in infants and young children.Am. J .radiol.1978:130:29-33.

12. Osborene D, White P, Radiology of epidemic adenovirus in infection of the lower respiratory tract in infants and young children. Am. J. roentgenology.1979:133:397-400.

13. Jay SJ, Johanson WG Pierce. The radiographic resolution of S.pneumonia.N.Engl.J.med.1975:293:798-801.

14. Subramanian L.Balachander A,Somu N,Elizabeth John,Narmadha R.Persistent and recurrent pneumonia-presented at the national conference of IAP, Jodhpur:Oct,1988.

15. Wald ER, Recurrent and non resolving pneumonia in children. semin. resp.infect.1993.8:46-58.

16. Rome L, Murali G. Lippman M.Non-resolving pneumonia and mimics of pneumonia.Med. clinics of N.america.2001.nov.85(6)1511-30.

17. Slowly resolving pneumonia. Oren Lasker.c.390.p.1435. In Nelson's textbook of paediatrics,17th ed.eds.Berhmann, Kleigmann, Jenson. WB saunders:El sevier.

18. Harrison's principles of internal medicine, eds. Kasper, Braunwald, Fauci, Hauser, Longo, Jameson. 16th ed,c:239:p.1528-29

19. Adopted from childhood resp .infections. British med bulletin. vol. 61. 2002. p.118. Oxford Univ.press.

20. Colombo JL, Samment PH, Aspiration syndromes. in pead resp. medicine. ed. Taussig LM, Landau, St.Louis.Mosby.1999.p.435-443.

21. Cook SP, Lawless S, Mandell GA, Reilly.The use of salivagram in the evaluation of severe and chronic aspiration. Int. J. of Otorhinology.1997: 41:353-361.

22. Kabra SK, Kabra M, Ghosh M, Verma,Cystic fibrosis and Indian perspective of recent advances in diagnosis and management. Ind. J. Paedtr.1998:63-189-198.

23. Charles G Prober, Pneumonia. In Nelson's textbook of peadiatrics.17th ed.p.1432-1435.WB Saunders.

24. Stokes DL. Resp. infn. in immunocompromised host. In Paed. resp. medicine. ed. Taussig EM.Landau CV.Mosby.1999.p.664-681.

25. Eigen E Lauglin J, Homigrausen J, Rec. pneumonia in children and its relation to bronchial hyper-reactivity.Paediatrics.1982:70:698-704.

26. Adam KR.Persistent / recurrent pneumonia in Saudi children seen at King Khalid university hospital, Riyadh. Clinical profile and some predisposing factors. Ann of trop. Paediatrics.1991:11:129-135.

27. Kumar KG, Bakshi S, Samantraj JC, Bannerji, Arya LS. Indian paedtr. 2004. vol 71:Issue:2:p.129-132.

28. Lodha K, Puranik M, Chandru V, Natchu M, Kabra SK, Persistent pneumonia in children. Ind. paedtr:2003:Oct.40:P 967-970.

29. Emmons CW et al., Medical mycology.3rd ed.eds. London, Harry Kimpton :1987.

30. Rubin BK.The evaluation of the child with rec. chest infn., Paed inf diseases.J.1985:4:88-96.

31. Kuru T, Lynch P et al,. Non- resolving or slowly resolving pneumonia. Clin. chest medicine:1999:Sep.20(3):623-651.

32. Victor Churnik, Thomas F Brat, Infections of the resp tract .In Kendig's disorders of the resp tract in children.6th ed:1998:p.415-562.

33. Colombo JL, Hallberg TK, Rec aspirations in children. Lipid laden macrophages and quantification. Paed pulm:1987:3:86-89.

34. Balachandran A, Shivbalan So. Evaluation of Persistant /Recurrent pneumonia in children.IJPP.2002:4(1)30-37.

35. Exploratory puncture of the chest. Abuse of the needle- A warning. British J. of child diseases.2:466:1905.

36. Horden J, Lung puncture. A new application of Clin. Pathlogy. Lancet: 2:1435:1909.

37. Lyon AD, Bacteriological study of one hundred and sixty five cases of pneumonia. Am. J. dis. child.23:72:1922.

38. Sappington BW. Favorite. Lung puncture in lobar pneumonia. Am. J. med. sciences.191:225:1936.

39. Mimica J, Donasa E, Howard JE, Lederman. Lung puncture in the etiological diagnosis of pneumonia. Am. J. dis. Child.4:122:1971.

40. Sakuntala SK, Mallikarjuna, Urmila S, Diagnosis by lung puncture in pneumonia of new born. Ind. paediatrics.14:39:1978.

41. Elina, Halopainen, Eava Salo, Maija Leinoven, Harri saxen, Etiological diagnosis of childhood pneumonia by transthoracic needle aspiration. Paed. pulm. Jan 98-1(7)211-216.

42. Berger Arango L, Value and safety of percutaneous lung aspiration. Paed pulm.1985:nov-dec.1(6)309-313.

43. Walter Pegoli, George T Drugas, Lung biopsy. In textbook of paedtric surgery. ed. Peter Mattei, Lippincott William and Wilkins, Philadelphia 2002

44. J. thoracic imaging.1997:Klein JS et al, Transthoracic needle biopsy. An overview.12:232-264.

45. Isenberg HD et al. manual of clinical microbiology ed.5, washington DC,1991. American society for microbiology.